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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/534,171	05/06/2005	Paola Branduardi	3912.1000-000	5195
21005 7590 12/13/2007 HAMILTON, BROOK, SMITH & REYNOLDS, P.C. 530 VIRGINIA ROAD P.O. BOX 9133 CONCORD, MA 01742-9133			EXAMINER VOGEL, NANCY S	
			ART UNIT 1636	PAPER NUMBER
			MAIL DATE 12/13/2007	DELIVERY MODE PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/534,171	BRANDUARDI ET AL.	
	Examiner	Art Unit	
	Nancy T. Vogel	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on ____.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 22-42 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 22-37 and 39-42 is/are rejected.
- 7) ☒ Claim(s) 38 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. ____.
3. ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|--|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>5/6/05</u> . | 6) <input checked="" type="checkbox"/> Other: <u>sequence alignment attachment</u> . |

DETAILED ACTION

Claims 22-42 are pending in the case.

Receipt of the Information Disclosure Statement on 5/6/05 is acknowledged.

Election/Restrictions

Applicant's election of the species of SEQ ID NO:1 and SEQ ID NO:69 in the reply filed on 9/19/07 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Drawings

New corrected drawings in compliance with 37 CFR 1.121(d) are required in this application because the drawings that show blot results contain dark background that makes their interpretation difficult or impossible. Applicant is advised to employ the services of a competent patent draftsman outside the Office, as the U.S. Patent and Trademark Office no longer prepares new drawings. The corrected drawings are required in reply to the Office action to avoid abandonment of the application. The requirement for corrected drawings will not be held in abeyance.

Priority

Receipt is acknowledged of papers submitted under 35 U.S.C. 119(a)-(d), which papers have been placed of record in the file.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 22 and 40 are rejected under 35 U.S.C. 102(b) as being anticipated by Radler et al. (J. Gen. Microbiol., 1993, 139:495-500).

Radler et al. disclose a method of producing a protein comprising culturing a *Zygosaccharomyces bailii* strain, expressing and secreting a protein, and isolating the protein from the culture medium (see abstract, see page 496, first column, first paragraph).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 22-26, 28-31, 34, 36, 37, 39-42 are rejected under 35 U.S.C. 103(a) as being unpatentable over Brambilla et al. (WO 00/41477) (cited by applicants) in view of (Brake et al., Proc. Natl. Acad. Sci. USA, 81, 4642-4646, 1984).

Brambilla et al. disclose method for production of a protein comprising the steps of culturing a *Zygosaccharomyces bailii* (*Z. bailii*) strain, expressing a protein such as a recombinant protein, and isolating the protein (see page 11, line 22-28). The reference discloses that appropriate sequence may be used for secretion (see page 3, lines 15-24). The reference discloses using an extra-chromosomal plasmid, derived from an endogenous episomal plasmid from *Z. bailii* strain, including sequences for replication, stabilization or plasmid copy number control (see claims, see Example 1-2). The reference discloses that the TPI (triphosphate isomerase) or the GAP (glyceraldehyde phosphate dehydrogenase) promoter of *S. cerevisiae* may be used (page 12 line 17-20). The reference discloses that strains such as ATCC 36947 or ATCC 60483 may be used (page 11 lines 20,21). The reference discloses that the DNA sequence coding for protein may be derived from any prokaryote or eukaryote (page 11 lines 22- page 12 line 16). The reference discloses that the strain may be cultivated in chemically defined medium (page 15).

The difference between the reference and the instant claims is that the protein is secreted and a signal sequence such as the signal sequence shown in SEQ ID NO:1, is operably linked to the DNA encoding the protein.

However, Brake et al. disclose the signal or prepro-sequence of the alpha factor mating pheromone encoding gene and its use to direct secretion of heterologous genes in yeast. It would have been obvious to have utilized a well known signal sequence such as that obtained from the alpha-factor encoding gene of the *S. cerevisiae* as disclosed by Brake et al., since the Brambilla et al. reference clearly suggests the use of standard

expression sequences for direction of the secretion of proteins of interest, and since Brake et al. discloses such as sequence for use in yeast. One would have been motivated to do so by the desire to secrete a protein from the *Z. bailii* yeast disclosed as useful by Brambilla et al., since secreted proteins are free of contamination by host proteins, and since their purification is normally easier than proteins contained within a cell. Based upon the teachings of the cited references, the high skill of one of ordinary skill in the art, and absent evidence to the contrary, there would have been a reasonable expectation of success to result in the claimed invention.

Claim 27 is rejected under 35 U.S.C. 103(a) as being unpatentable over Brambilla et al. (WO 00/41477) (cited by applicants) in view of (Brake et al., Proc. Natl. Acad. Sci. USA, 81, 4642-4646, 1984) as applied to claims 22-26, 28- 31, 34, 36, 37, 39-42 above, and further in view of Jacobson et al. (WO9204461).

Brambilla et al. and Brake et al. are cited essentially for the reasons set forth above.

The difference between the references and the instant claim is that a particular DNA sequence, ie. at least 35 nucleotides of the sequence that is shown in SEQ ID NO:69, is present in the plasmid.

However, Jacobson et al. disclose a DNA sequence which comprises at least 35 nucleotides of the sequence shown in SEQ ID NO:69 (see alignment attached). Jacobson et al. disclose that the DNA encodes a particular antigen. It would have been obvious to one of ordinary skill in the art to have placed the DNA disclosed by Jacobson et al. in the plasmid and strain disclosed by Brambilla et al. and Brake et al., since

Brambilla disclose that any DNA encoding a protein of interest may be expressed in the disclosed yeast strains, and since Jacobson disclose such a DNA encoding a protein of interest. One would have been motivated to do so by the disclosure of Brambilla et al. which discloses that the *Z. bailii* yeast has certain advantages for the expression of proteins of interest, and since Jacobson et al. disclose such a protein which is useful for production of antigens of a organism of economic importance. Based upon the teachings of the cited references, the high skill of one of ordinary skill in the art, and absent evidence to the contrary, there would have been a reasonable expectation of success to result in the claimed invention.

Claim 32 is rejected under 35 U.S.C. 103(a) as being unpatentable over Brambilla et al. (WO 00/41477) (cited by applicants) in view of (Brake et al., Proc. Natl. Acad. Sci. USA, 81, 4642-4646, 1984) as applied to claims 22-26, 28- 31, 34, 36, 37, 39-42 above, and further in view of Stark et al. (EMBO J., 5, 1995-2002, 1986).

Brambilla et al. and Brake et al. are cited essentially for the reasons set forth above.

The difference between the references and the instant claim is that a particular signal sequence, i.e that from the alpha-subunit of the K1 killer toxin of *K. lactis*, is used. However, Stark et al. Disclose the signal sequence of the alpha-subunit of the K1 killer toxin of *K. lactis*, and its function in directing the secretion of a protein product operably linked. It would have been obvious to one of ordinary skill in the art to have placed the signal sequence of Stark et al. in operable linkage to a protein of interest and a

promoter of interest, since Brambilla et al. disclosed that appropriate sequences for the localization of a protein of interest may be used, and since Stark et al. disclose such a sequence for secretion of a protein of interest. One would have been motivated to do so by the desire to obtain secreted, and therefore more easily purified, heterologous proteins. Based upon the teachings of the cited references, the high skill of one of ordinary skill in the art, and absent evidence to the contrary, there would have been a reasonable expectation of success to result in the claimed invention.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 33, 35 and 37 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

It is apparent that plasmids and strains required to practice the invention as claimed. As such, the plasmids and strains must be readily available or obtainable by a repeatable method set forth in the specification, or otherwise readily available to the public. If it is not so obtainable or available, the requirements of 35 U.S.C. 112, first paragraph, may be satisfied by a deposit of the plasmid. In the instant case, the

process to generate the plasmids and strains that is disclosed in the specification does not appear to be repeatable, nor does it appear the plasmids and strains are readily available to the public.

If a deposit is made under the terms of the Budapest Treaty, then an affidavit or declaration by Applicants, or a statement by an attorney of record over his or her signature and registration number, stating that the instant invention will be irrevocably and without restriction released to the public upon the issuance of a patent, would satisfy the deposit requirement made herein. If a deposit has not been made under the Budapest Treaty, then in order to certify that the deposit meets the criteria set forth in 37 CFR 1.801-1.809 and MPEP 2402-2411.05, Applicant may provide assurance of compliance by affidavit or declaration, or by a statement by an attorney of record over his or her signature and registration number showing that:

- a) during the pendency of the application, access to the invention will be afforded to the

Commissioner upon request;

- b) all restrictions upon availability to the public will be irrevocably removed upon the granting of the patent;

- c) the deposit will be maintained in a public depository for a period of 30 years, or 5 years after the last request for the enforceable life of the patent, whichever is longer;

- d) a test of the viability of the biological material at the time of deposit (see 37 CFR 1.807); and

- e) the deposit will be replaced if it should ever become inviable.

Failure to make one of the preceding indications in response to this Office Action will result in the rejection being maintained in either a second Non-Final or a Final rejection.

Claim 38 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nancy T. Vogel whose telephone number is (571) 272-0780. The examiner can normally be reached on 7:00 - 3:30, Monday - Friday.

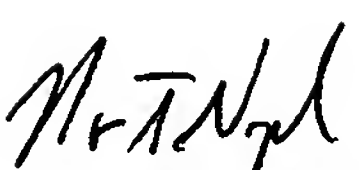
If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Voitach can be reached on (571) 272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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NTV
12/7/07


NANCY VOGEL
PRIMARY EXAMINER

<!--StartFragment-->RESULT 3

AAQ23082/c

ID AAQ23082 standard; DNA; 417 BP.

XX

AC AAQ23082;

XX

DT 25-MAR-2003 (revised)

DT 17-AUG-1992 (first entry)

XX

DE Antigen tc-11e gene.

XX

KW Oocysts; immune bile; mucosal immune response; chicken; parasite; ss.

XX

OS Eimeria tenella.

XX

PN WO9204461-A.

XX

PD 19-MAR-1992.

XX

PF 05-SEP-1991; 91WO-US006431.

XX

PR 12-SEP-1990; 90US-00581694.

XX

PA (GEMX) GENEX CORP.

PA (FARH) HOECHST AG.

XX

PI Jacobson JW, Strausberg RL, Wilson SD, Pope SH, Strausberg SL;

PI Raether W;

XX

DR WPI; 1992-114366/14.

DR P-PSDB; AAR22382.

XX

PT Vaccine against avian coccidiosis - comprising recombinant eimeria
 PT antigen mc-4c, mc-5c or mc-30c gene, etc., or microorganisms expressing
 PT them.

XX

PS Claim 11; Page 65 + Fig 11; 94pp; English.

XX

CC To identify antigens of E. tenella that elicit a mucosal immune response
 CC during parasitic infection of chickens, E. tenella cDNA and genomic
 CC expression libraries in lambda phage were screened with chicken immune
 CC bile. Phage that produce antigens cross-reactive with the immune bile
 CC were identified. The DNA inserts from the positive phage were cloned into
 CC bacteriophage M13 and subjected to sequence analysis. E. tenella antigen
 CC tc-11e was identified. (Updated on 25-MAR-2003 to correct PA field.)

XX

SQ Sequence 417 BP; 103 A; 127 C; 138 G; 49 T; 0 U; 0 Other;

Query Match 34.1%; Score 39.6; DB 2; Length 417;

Best Local Similarity 66.3%; Pred. No. 2.1;

Matches 57; Conservative 0; Mismatches 29; Indels 0; Gaps 0;

Qy 5 CTGCACGTGCCACCGGAGGTGCTGTGGGAGCGACTGCGGCACGATCGCCATCGGCCGCTG 64
 |||| ||| | || | |||| || || |||| | | | | ||||
 Db 103 CTGCTGCTGCTGCAGGTGCTGCTGCTGGTGCTGCTGCTGGCGGCGCTGCTGCTGCTGCTG 44

Qy 65 CTGCAGGTGCCGAGCCGAGGCAGCG 90
 |||| |||| |||| |||| |||| ||||
 Db 43 CTGCTGGTGAGCAGCCGAGGGCGCG 18

<!--EndFragment-->